UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Note to Reader
August 7, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply, EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, if unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues

available in the information in this docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack Housenger, Acting Director
Special Review and Reregistration
Division

September 29, 1995

MEMORANDUM

SUBJECT: **ETHION: REVISED** HED Chapter of the Reregistration Eligibility Decision Document (RED), Case #0090

From: Jane Smith, Chemist
Risk Characterization and Analysis Branch
Health Effects Division 7509C

Thru: Stephanie Irene, Ph.D., Acting Director
Health Effects Division 7509C

To: Walter Waldrop
Reregistration Branch
Special Review and Reregistration Branch 7508

The Human Health Assessment for the Reregistration Eligibility Document for ethion was originally completed 9/7/94. SRRD incorporated this chapter into a draft RED document which was forwarded to the registrant to facilitate risk mitigation discussions. Risk mitigation and rebuttal information was provided by the Registrant in response to the draft RED. It soon became clear that due to risk mitigation and some policy changes in HED that HED's chapter for this chemical needed to be revisited and a documented revision of the chapter generated.

The most significant revisions include:

- -additional reductions in the use rate which changed the occupational exposure and risk determinations,
- -reevaluated toxicological endpoints,
- -inclusion of a dermal absorption factor for worker risk assessment,
- -further refinement of residues levels for acute dietary risk assessment.

Based on these revisions, the risk remains a concern for workers for all scenarios. The acute dietary risk is a concern for the major population subgroups except males 13+ years. The chronic dietary risk is not unreasonable. There are no residential uses.

B. Human Health Assessment

1. Toxicology Assessment

The toxicological data base is adequate and will support reregistration. Some confirmatory data (GL#s 81-8, 82-7, and 85-1) are however required to maintain the continued registration of ethion (See discussion under B.1.h and B.1.k).

a. Acute Toxicity

The acute toxicity data on technical ethion are summarized in the table below:

Table I: Acute Toxicity of Ethion Technical

GL# - Study	Results	Category	MRID#
81-1 Oral LD_{50} (rat)	191 mg/kg (M) 21 mg/kg (F)	I	00157590
81-2 Dermal LD_{50} (rat)	838 mg/kg	II	00157590
81-3 Inhalation LC_{50} (rat)	2.31 mg/L (M) 0.45 mg/L (F)	II	00163159
81-4 Eye Irritation (rabbit)	slight redness	IV	00157590
81-5 Dermal Irritation (rabbit)	slight erythema	IV	00157590
81-6 Dermal Sensitization (guinea pig)	negative	N.A.	00141205
81-7 Acute Neurotoxicity (hen)	negative	N.A.	00158376

b. Subchronic Toxicity

The requirement for a subchronic oral toxicity study in rodents (GL# 82-1) is satisfied by a 2-year chronic/carcinogenicity feeding study in rats (MRID# 00148991).

In a 90-day oral toxicity study in dogs (GL# 82-1), ethion was administered in the diet to beagle dogs at concentrations of 0, 0.5, 2.5, 25.0, or 300 ppm (0.0125 to 7.5 mg/kg/day). The systemic toxicity NOEL was 25 ppm (0.71 mg/kg /day) and the LOEL was 300 ppm (6.9 mg/kg/day in males, 8.25 mg/kg/day in females), based on reductions in body weight gain and food consumption and on clinical signs of toxicity--ataxia, emesis, miosis and tremors.

The NOEL for cholinesterase (ChE) inhibition was 0.5 ppm (0.01 mg/kg/day). The LOELs for inhibition of plasma, brain, and erythrocyte ChE activities were 2.5 ppm, 25 ppm, and 300 ppm, respectively (MRID# 40773301).

Two 21-day dermal toxicity studies were conducted with ethion in rabbits (GL# 82-2). In one study, the doses were 0, 1.0, 3.0, 25, or 250 mg/kg/day. Erythema and desquamation at the application sites occurred in both sexes at doses of 25 mg/kg/day (systemic LOEL) or more, and inhibition of ChE activity in plasma, red cells, and brain occurred at 1 mg/kg/day or more. The NOELs for systemic toxicity and ChE inhibition were 3 mg/kg/day and less than 1 mg/kg/day (lowest dose tested), respectively (MRID 00155498). A second study with New Zealand white rabbits included lower doses of ethion at 0, 0.1, 0.25, 0.5, 0.8, 1.0, 3.0, or 25 mg/kg/day. Inhibition of brain ChE activity occurred at 1 mg/kg/day or more (MRID 00155499). When the results of the 2 dermal studies were combined, the NOEL for ChE inhibition was established at 0.8 mg/kg/day.

c. Chronic Toxicity

The requirement for a chronic oral toxicity study in rodents (GL# 83-1) is satisfied by a 2-year chronic/carcinogenicity feeding study in rats (MRID# 00148991) discussed below.

In a chronic oral toxicity study (GL# 83-1), ethion was administered in the diet for one year to beagle dogs at concentrations of 0, 0.5, 1.0, 2.0, 20, or 100 ppm (approximately 0, 0.011, 0.026, 0.049, 0.52, or 2.53 mg/kg/day for males and 0, 0.011, 0.028, 0.053, 0.53, or 2.56 mg/kg/day for females). The NOEL was 1.0 ppm. The LOEL was 2 ppm, based on dose-related and statistically significant decreases in plasma ChE activity at this and higher doses. Erythrocyte ChE activity was decreased at higher doses (20 ppm in females). Both erythrocyte and brain ChE activities were decreased at 100 ppm (MRID# 41188401).

d. Carcinogenicity

In a chronic/carcinogenicity feeding study (GL#s 83-1 and 83-2), Sprague-Dawley rats were fed diets containing 0, 2, 4, or 40 ppm ethion (0.1 to 2.0 mg/kg/day) for 24 months. The only effects observed were reductions in serum ChE activity at 40 ppm, which occurred in females at 6, 12 and 18 months and in males at 12 and 18 months. The NOEL for ChE inhibition was 4 ppm (0.2 mg/kg/day) and the systemic toxicity NOEL exceeded 40 ppm (HDT). No carcinogenic effects were observed (MRID# 00148991).

In a carcinogenicity feeding study (GL# 83-2), CF1 mice were fed diets containing 0, 0.75, 1.5, or 8.0 ppm ethion (0.11 to 1.2 mg/kg/day) for 2 years.

The systemic NOEL was 1.5 ppm (0.225 mg/kg/day) and the LOEL was 8 ppm for both sexes, based on decreased plasma ChE activity. No carcinogenic effects were observed; tumor incidence was comparable between treated and control animals (MRID# 00148989).

Ethion is classified as a "Group E" carcinogen (evidence of non-carcinogenicity for humans) based on the available data.

e. Developmental Toxicity

In a developmental toxicity study (GL# 83-3), Charles River rats were gavaged with 0, 0.2, 0.6 or 2.5 mg/kg/day ethion on gestation days 6-15. Both the maternal and developmental toxicity NOELs were 0.6 mg/kg/day. Both the maternal and developmental toxicity LOELs were 2.5 mg/kg/day, based on signs of hyperactivity in the parents and on delayed ossification of pubes in the fetuses (MRID# 00131852).

In another developmental toxicity study (GL# 83-3), New Zealand white rabbits were administered 0, 0.6, 2.4 or 9.6 mg/kg/day ethion by gavage on gestation days 6-18. The NOEL for maternal toxicity was 2.4 mg/kg/day and the LOEL was 9.6 mg/kg/day due to weight loss, reduced food consumption, and orange colored urine. The NOEL for developmental toxicity was the highest dose tested (MRID# 00131853).

f. Reproductive Toxicity

In a three-generation study (GL# 83-4) in which ethion was fed to Charles River rats at concentrations of 0, 2, 4 or 25 ppm, the reproductive NOEL was 25 ppm (1.25 mg/kg/day), the highest dose tested. The systemic toxicity NOEL was 25 ppm in male rats and 4 ppm (0.2 mg/kg/day) in F_1 and F_2 female rats due to a decrease in serum ChE activity at the highest concentration (MRID# 00148990).

g. Mutagenicity

Results of mutagenicity studies indicate that ethion does not appear to be mutagenic. The results of these studies are summarized in the table below:

Table II: Mutagenicity Studies with Ethion

Study Type	GL #	Results
Gene Mutation/Ames	84-2a	Negative, w/wo metabolic activation, at ≤ 10000 ug/plate (MRID# 00144351) or at ≤ 20000 ug/plate (MRID# 00096523).
Structural Chromosome Averration (in-vivo cytogenic test/rats	84-2b	Negative in male rats treated with 4.7, 14, 47, or 140 mg/kg/day (MRID# 00142546).
Unscheduled DNA Synthesis in-vitro (rat hepatocytes)	84-4	Negative at levels of 0.625, 1.25, 2.5, 5.0, or 10 ng/ml. (MRID# 00142545)
Recombinant/conversion assay in S. cerevisiae	84-4	negative, w/wo metabolic activation at ≤ 10% v/v (i.e. 10000ppm)(MRID# 00096522)

h. Metabolism

Metabolism data are not available. Confirmatory metabolism studies with ethion are required for the continued registration of ethion.

i. Human Special Toxicity Study

Ten male adult human volunteers were used in a study in which ethion was orally administered for 21 days at dose levels of 0.05, 0.075, 0.10 or 0.15 mg/kg/day. No consistent effects on plasma or erythrocyte ChE activity were observed at 0.05 mg/kg/day, originally the NOEL and reclassified as the LOEL since effects were observed on the 19th day of treatment. Statistically significant reductions in plasma ChE activity, which ranged from -15% to -31%, were observed at doses of 0.075 to 0.15 mg/kg/day. Erythrocyte ChE activity was not affected (MRID 00073157). **On August 31, 1995, the HED RfD Committee reevaluated the study and determined that 0.05 mg/kg/day is the LOEL (see discussion in the Dose Response section under RfD).**

j. Other Toxicological Considerations

Ethion is an organophosphorus chemical which consistently produces ChE inhibition in both human and animal studies (MRID#s 00073157, 40773301, 00155498, 00155499, 41188401, 00148991, 00148989, and 00148990). Administration of ethion to animals is associated with neurotoxic signs of ataxia, tremors (MRID# 40773301), and hyperactivity (MRID# 00131852). Based on the chemical structure of ethion and these adverse effects, the Agency will require both an acute and a 90-day neurotoxicity study in rats, conducted according to EPA's newly revised neurotoxicity guidelines (81-8 and 82-7). Although these data

requirements are not part of the reregistration data base, they are needed for the continued registration of ethion.

Ethion has been cited in numerous pesticidal poisoning incidents. Between 1976 and 1985, ethion was the 8th most frequent cause of reentry poisonings in California. EPA's Incident Data System (IDS) contains information on adverse reactions to ethion; for the reporting period of April 1992 to July 1993, three data entries contained a total 116 incidents. Most of the incidents pertain to humans, but some include cattle and domestic animals.

2. Dose Response Assessment

a. Reference Dose

In 1994, the RfD was established for ethion at 0.0005 mg/kg/day, based on the human study (MRID# 00073157), with a plasma cholinesterase inhibition NOEL of 0.05 mg/kg/day and a safety factor of 100 . Both the subchronic (MRID 40773301) and chronic toxicity studies in dogs (MRID# 41188401) were used as co-critical studies, since the critical effect, plasma ChE inhibition, occurred in the same dose range. Brain ChE inhibition was also observed in the dog studies (NOEL/LOEL = 0.06/0.71 mg/kg/day in males in subchronic study; and = 0.049/0.52 mg/kg/day in chronic study). The safety factor of 100 included a factor of 10 to account for the difference in sensitivity within the human population and an additional factor of 10 to account for brain cholinesterase inhibition, observed in the co-critical dog studies.

The HED/RFD Peer Review Committee reconvened on August 31, 1995 to re-examine the toxicity database of ethion with particular reference to the following:

- The oral 21-day study in humans (MRID No. 00073157, previously reviewed by the Agency in HED Doc. 007033, August 30, 1983)
- The published experimental value for human dermal absorption of ethion [Toxicol. Appl. Pharmacol. 28: 126-132 (1974)]3 and
- The 21-day rabbit dermal toxicity data (MRID Nos. 00155499 and 00155498).

Upon re-evaluation of the results of the 21-day oral study in humans, the HED/RFD Peer Review Committee concluded that the study defined a LOEL of 0.05 mg/kg/day (the lowest dose tested), the NOEL was undefined in this study. This conclusion was based on the appearance of clinical signs of cholinesterase inhibition in one subject towards the end of the low-dose (0.05 mg/kg/day) administration period and in another subject on the first day of the next higher dose

period (0.075 mg/kg/day). The first subject reported headache and blurred vision on days 19-21 of the low-dose period and on day 1 of the 0.075 mg/kg/day period; lightheadedness and dizziness were reported by this subject on the following day. The second affected subject reported partial blindness and lightheadedness twice on the first day of receiving 0.075 mg/kg/day and on the first day of receiving 0.15 mg/kg/day. These results show the occurrence of cholinergic signs in 2 out of 6 subjects and taken together, can be interpreted as a reflection of a cumulative effect of the test material administered at the dose of 0.05 mg/kg/day and higher doses.

It is noted that in the initial review of the 21-day oral study in humans, the reviewer had discussed the cholinergic symptoms presented by the two subjects but had concluded that the symptoms were not treatment-related. Thus, the LOEL was defined, at that time, as 0.075 mg/kg/day based on inhibition of plasma cholinesterase activity with a NOEL of 0.05 mg/kg/day. In the present re-evaluation of the study the HED/RFD Peer Review Committee felt that the cholinergic signs are sufficiently consistent in the two subjects to indicate a treatment-related effect at the low dose.

The HED/RFD Peer Review Committee concluded that to establish the RfD an uncertainty factor of 10 be used to account for the lack of a NOEL and an additional uncertainty factor of 10 be used to account for the differences in sensitivity within the human population. **On this basis the RfD was maintained at 0.0005 mg/kg/day.**

b. Carcinogenicity Classification

Ethion is classified as a "Group E - evidence of noncarcinogenicity for humans" based on the available data.

c. Other Toxicological Endpoints

Originally the toxicological endpoint for the occupational and residential risk assessments was a NOEL of 0.8 mg/kg/day based on a 21-day dermal study conducted with rabbits (MRID# 00155499). In a document dated August 3, 1995 ["Ethion Exposure: Risk to Workers", no MRID number], FMC corporation disagreed with toxicological endpoint of 0.8 mg/kg/day (NOEL) from the 21 day rabbit dermal study [MRID Nos. 00155499 and 00155498]. FMC recommended that the 21-day oral human study (MRID# 00073157) was more appropriate with the dermal absorption factor from the published experimental value for human dermal absorption of ethion [Toxicol. Appl. Pharmacol. 28: 126-132 (1974)] submitted with the August 3rd document. On August 31, 1995 the RfD Committee considered the registrants's position and established the following

toxicological endpoints:

i. Acute Dietary

The acute dietary endpoint is the LOEL of 0.05 mg/kg/day from the human study (MRID# 00073157), based on clinical signs of cholinesterase inhibition. Generally an MOE of 10 is appropriate for risk assessment when the toxicological endpoint is based on a human study. Since this human study has a LOEL and no NOEL then an MOE of 100 should apply; however, since the effects were seen in the study on the 19th day an MOE of 10 is appropriate for the acute dietary, 1 day type exposure.

ii. Dermal Absorption

In the evaluation of the published experimental value for human dermal absorption of ethion [Toxicol. Appl. Pharmacol. 28: 126-132 (1974)] it was concluded that the absorption value of 6.6% of the dose (i.e. the reported mean 3.3% plus 3 standard deviations, which encompasses most of the population) is adequate for risk assessment purposes.

iii. Short and Intermediate Term Occupational and Residential

The HED RfD Peer Review Committee (August 31, 1995) recommended the LOEL of 0.05 mg/kg/day from the human study (MRID# 00073157), based on clinical signs of cholinesterase inhibition. The Committee re-examined the 21-day rabbit dermal toxicity data (MRID Nos. 00155499 and 00155498) and noted that the data suggest that after dermal dosing with ethion, rabbit brain cholinesterase is significantly inhibited at lower doses than those required to inhibit significantly plasma and erythrocyte cholinesterase. It was also noted that these results contrast with findings in oral studies with rats and dogs that show significant inhibition of plasma and erythrocyte cholinesterase at lower ethion doses than those required to inhibit brain cholinesterase significantly. The Committee concluded that it was unclear, with the available data, whether the effect observed in the 21-day rabbit dermal study reflected a route effect valid for other species or was a species specific effect. Therefore, the LOEL from the human study is the most appropriate endpoint.

Further, an MOE of 100 was recommended; a factor of 10 is based on the lack of a NOEL and an additional factor of 10 accounts for the differences in sensitivity within the human population. In the case of ethion, the use of an MOE of 100 when using an oral study is additionally supported by the results of the 21-day dermal rabbit study, which suggest that upon dermal dosing, brain cholinesterase may be inhibited at lower doses than plasma or erythrocyte cholinesterase.

3. Occupational and Residential Exposure and Risk Characterization

a. Occupational and Residential Exposure

This occupational and residential exposure and risk characterization includes risk mitigation from the registrant that reduced the maximum label application rate and proposed enclosed cabs for the airblast applications.

Ethion is used on citrus to control Citrus Red Mite, Citrus Rust Mite, Sixspotted Mite, Texas Citrus Mite, Citrus Whitefly and Blackfly, Snow Scale, Black Scale, Brown Soft Scale, California Red Scale, Chaff Scale, Florida Red Scale, Glover Scale, Purple Scale, and Yellow Scale. End-use product formulations for citrus use consist of emulsifiable concentrates (EC), containing from 9% to 81.9% active ingredient.

Applications can be made using ground boom, or airblast equipment. In addition, high-pressure and low-pressure hand wands along with backpack sprayers may be used for various applications such as spot treatments. Maximum application rates were originally 7.5 lb a.i./A and mitigated to a maximum of range up to 2.5 lb a.i./A. The exposure assessment is based on the maximum of 2.5 lb a.i./A. Based on the existing information, there appears to be no residential indoor/outdoor uses for ethion.

Exposure - Mixer/Loader/Applicator

Mixer/loader/applicator (i.e., handler) exposure study requirements are addressed by Subdivision U of the Pesticide Assessment Guidelines. Mixer/loader/applicator (M/L/A) exposure data (i.e., GL#s 231 and 232: outdoor dermal and inhalation, and GL#s 233 and 234: indoor dermal and inhalation), involving several use patterns (terrestrial food, terrestrial non-food, greenhouse non-food, and domestic outdoor) were required by the 1989 *Registration Standard for Products Containing Ethion*. The required data have not been submitted by the registrant. However, because the registrants are maintaining only the citrus use, only data for Guidelines 231 and 232 for citrus are currently required.

Based on ethion pattern of use, several exposure scenarios are plausible as defined by the types of application equipment and procedures that might be employed by ethion handlers. Each scenario is presented in the **Summary Exposure Value Table** along with a corresponding exposure assessment (Table V). Typical equipment used to treat citrus crops serve as the basis of this assessment. Exposure estimates were derived from the PHED. All exposure values were based as closely as possible on the clothing/PPE scenario required for ethion by the Worker Protection Standard (WPS). Ethion is category II for both acute dermal and inhalation toxicity. As a result, the WPS standard requires, at a minimum, "coveralls worn over a short-sleeved shirt and short pants", chemical resistant gloves, a "chemical resistant apron when cleaning equipment, mixing or loading", and a respirator be worn.

To clarify the **Summary Exposure Value Table** (Table III, V), the **Exposure**

Scenario Description Table (Table IV) was developed. Table IV summarizes the caveats and parameters specific to each exposure scenario. This table also includes a description of the sources for each data point as well as general information pertaining to the techniques used to calculate the corresponding exposure values. The quality of the data for each exposure scenario is also addressed.

For several scenarios, exposure data for the exact clothing requirements as stipulated by the WPS were not available. As a result, standard protection factors were applied to the available data for each scenario to "normalize" the data in order to, as closely as possible, represent the WPS clothing scenario. The **Clothing Scenario** presented in Table IV indicates the clothing upon which the exposure value was developed prior to any "normalization" procedure. The normalization process is based on the following assumptions:

- Unless otherwise indicated, hand exposure accounts for 50 percent of the total dermal exposure while non-hand exposure accounts for the remaining 50 percent,
- Gloves have a protection factor in the range of 50 percent - 90 percent (for purposes of this document 50 percent protection factor will be used as a conservative estimate),
- Normal work clothing has a protection factor of 50 percent,
- Pilot assessments are based solely on the use of normal work clothing with no protective gloves,
- Normal work clothing is considered for the purposes of these calculations as any combination of short- or long-sleeved shirt and short or long pants,
- Coveralls have a protection factor of 50 percent, and
- Disposable dust/mist masks have a protection factor of 80 percent.

In the 1989 Registration Standard, mixer/loader/applicator exposure data were required by the Agency because ethion met triggers for the requirement of exposure data (i.e., toxicity endpoint and the potential for significant exposure based on the use pattern). A document entitled "Biomonitoring Risk Assessment and Margin of Safety Risk Assessment Based on Surrogate Exposure Models for Workers Treating Citrus with Ethion Insecticide/Miticide in Airblast Sprayers" (EPA MRID 417160-01) was submitted to the Agency in support of Subdivision U requirements for the reregistration of ethion:

This submission did not meet the acceptability criteria outlined in Subdivision U of

the Pesticide Assessment Guidelines. The Mixer/Loader/Applicator risk assessment is unacceptable because of the following major inadequacies:

- there was a general lack of organization and references,
- critical surrogate exposure data used in the risk assessment were not properly documented (i.e., several of the data sources used by the investigator were not available to the Agency for review and/or verification, the amount of chemical handled in the surrogate exposure studies was not verifiable, data manipulations completed by the investigator were not provided in the report),

- insufficient pharmacokinetics data were included in the submission, and

- it appeared the investigators selectively utilized available surrogate exposure data to potentially create a bias in the results of the assessment to decrease the anticipated hazards associated with the targeted uses of ethion.

Based on the toxicological endpoints (ChE inhibition), the potential for exposure, and the results of the hazard assessment presented in Table V, ethion continues to meet EPA's criteria for the requirement of mixer/loader/applicator exposure data. The following data are required for reregistration:

GL# 231 Estimation of dermal exposure at outdoor sites: Data are required for open cab airblast , high pressure handwand, knapsack/backpack, hose-end sprayer, and low pressure handwand application to citrus.

GL# 232 Estimation of inhalation exposure at outdoor sites: Data are required for open cab airblast, high pressure handwand, knapsack/backpack, hose-end sprayer, and low pressure handwand application to citrus.

These data are considered confirmatory only if the risk assessment does not indicate a significant risk to workers. Guideline numbers 233 and 234 (estimation of dermal/inhalation exposure at indoor sites) are not required since ethion has no indoor uses.

Table III: Summary Exposure Values Which Conform to the WPS Clothing/PPE Requirements For Ethion[a]

Exposure Scenario (Scen. #)	Unit Dermal Exposure[b] (mg/lb ai)	Unit Inhalation Exposure[b] (ug/lb ai)	Maximum Label Application Rate[c] (lb ai/acre)	Daily Maximum Treated[d] (acres) or (gallons/day)
Mixer/Loader Exposures[e]				
Open Mixing Liquids For Aerial Application (I)**	0.15	0.08	2.5	350
Open Mixing Liquids For Ground-Based Applications (II)	0.15	0.08	2.5	80
Applicator Exposures				
Groundboom Application (III)	0.01	0.26	2.5	80
Airblast Application (IV)**	1.35	0.84	2.5	17
Aerial Application (V)	0.005	0.04	2.5	350
High Pressure Handwand Application (VI)	0.53	0.018	2.5 lb ai/acre, (0.05 lb/gal)	2000 gal
Mixer/Loader/Applicator Exposures				
Mixing/Loading and Application with a Backpack Sprayer (VII)	1.93	6.04	2.5 lb ai/acre, (0.05 lb/gal)	80 gal
Mixing/Loading and Application with a Low Pressure Handwand Sprayer (VIII)	51.5	7.8	2.5 lb ai/acre, (0.05 lb/gal)	40 gal
Mixing/Loading and Application with a Hose-End Sprayer(IX)	25.20	0.002	2.5	2

[GENERAL NOTE: All unit exposure values presented in Table III have been "normalized", where appropriate (i.e., exceptions are noted in Table V), to reflect clothing scenario as described above. The WPS also requires a chemical resistant apron for mixing/loading activities.

a Units may differ from those defined in headers because of the type of equipment used, etc. Alternate units are noted where appropriate.

b All unit exposure values reflect the WPS clothing/PPE requirements for ethion [toxicity II dermal and inhalation pesticide/WPS = coveralls worn over short-sl and short pants, chemical resistant gloves, and a disposable dust/mist mask] except for scenario V (i.e., pilots). Assessments for both types of applicators are solely upon the use of normal work clothing with no gloves. All values are best fit results unless noted.

c Values represent FMC's indicated maximum application rate. Mixing/loading scenarios were based on the highest potential cumulative chemical use for all a methods included in this table in conjunction with the maximum number of acres treated for that application technique. Any estimates not provided as (lb ai/ac reported in that manner because for each particular application technique it is extremely difficult to estimate rate on a unit area basis as opposed to estimating t of spray solution applied.

d Values represent the maximum area (acres) or the maximum spray solution volume (gallons) which can be used in a single day to complete treatments for a equipment type/exposure scenario of interest.

e Reported mixer/loader exposure levels represent the maximum amount of chemical which can be handled on a daily basis. Therefore, the resultant exposur can not be directly added to exposure values for each application technique. Any additional daily exposure levels of interest must be calculated based on the ir included in the table.

** In FMC's "Ethion Risk Mitigation Proposal", the registrant proposed to prohibit aerial applications; if finalized, then this exposure scenario will not be applica

Table IV: Exposure Scenario Descriptions For Ethion

Exposure Scenario (Scen. #)	Data Source	Clothing Scenario	Equipment	Formulation(s)	Standard Assumptions[a] (8 hr workday)	Comments
Mixer/Loader Exposures[b]						
Open Mixing Liquids For Aerial Application (I)**	PHED	Long Pants, Long Sleeves, No Gloves	Open System	All Liquids	50% protection factor applied to both hand and dermal (nonhand) exposure to account for the use of protective gloves and a coverall	A/B grade PHED data, highest plausible ethion use scenario is for one mixer/loader to support a single pilot making applications to oranges, lemon, etc. (i.e., 2 pilots or 700 acres is unlikely for citrus) Dermal = 14 - 48 replicates Inhalation = 40 replicates (High confidence in the data)
Open Mixing Liquids For Ground-Based Applications (II)	PHED	Long Pants, Long Sleeves, No Gloves	Open System	All Liquids	50% protection factor applied to both hand and dermal (nonhand) exposure to account for the use of protective gloves and a coverall	A/B grade PHED data, Dermal = 14 -48 replicates Inhalation = 40 replicates (High confidence in the data)
Applicator Exposures						
Groundboom Application (III)	PHED	Long Pants, Long Sleeves, No Gloves	Open Cab Groundboom Tractor	All	50% protection factor applied to both hand and dermal (nonhand) exposure to account for the use of protective gloves and a coverall, number of treated acres based on judgement of OREB	A,B,C grade PHED data for dermal (nonhand) exposure; hand data mostly (50%) PHED grade D,E. Dermal = 6 - 54 replicates Inhalation = 56 replicates (Low confidence in the data)
Airblast Application (IV)	PHED	Coveralls, Gloves	Open Cab, Airblast Tractor	All	50% protection factor applied to dermal (nonhand) exposure to account for the use of normal work clothing worn underneath the protective coverall, number of treated acres based on judgement of OREB	A/B grade PHED data Dermal = 12 -19 replicates Inhalation = 24 replicates (High confidence in the data)
Aerial Application (V)**	PHED	Long Pants, Long Sleeves, No Gloves	All Aerial Cabs	All	No protection factor applied, number of treated acres based on judgement of OREB	All grade PHED data Dermal = 4 - 41 replicates Inhalation = 25 replicates (A,B,C grade data) (Low confidence in the data)
High Pressure Handwand Application (VI)	PHED	Long Pants, Long Sleeves, Gloves	All High Pressure Handwand	All	250 gallons/hour (value based on judgement of OREB and potential flow rate of sprayer type), 50% protection factor applied to dermal (nonhand) exposure to account for the use of a protective coverall	B/C grade PHED data Dermal = 9 replicates Inhalation = 9 replicates (Low confidence in the data
Mixer/Loader/Applicator Exposures						
Mixing/Loading/ Application with a Backpack Sprayer (VII)	PHED	Long Pants, Long Sleeves, Gloves	Backpack Sprayer	All	2 tankloads/hour (value based on judgement of OREB and potential flow rate for sprayer type), 50% protection factor applied to dermal (nonhand) exposure to account for coverall over the normal clothing	B grade PHED data for dermal (nonhand) exposure; hand data mostly (50%) PHED grade D,E. Dermal = 9 replicates Inhalation = 9 replicates (High confidence in the data)

Exposure Scenario (Scen. #)	Data Source	Clothing Scenario	Equipment	Formulation(s)	Standard Assumptions[a] (8 hr workday)	Comments
Mixing/Loading and Application with a Low Pressure Handwand Sprayer (VIII)	PHED	Long Pants, Long Sleeves, No Gloves	Low Pressure Handwand	All	2 tankloads/hour (value based on judgement of OREB, a potential flow rate of sprayer ... 2.5 gallon/tank ... protection factor applied to body ... exposure to account for the use of a protective coverall	B/C grade PHED data ... hand and dermal ... Dermal = 25 - 95 replicates ... Inhalation = 95 replic... (Low confidence in the...
Mixing/Loading and Application with a Hose-End Sprayer (IX)	PHED	Total Deposition	Typical Hose-End Sprayer	All	2 acres/day based on judgement of OREB, 50% protection factor applied to dermal (nonhand) exposure to account for use of typical work clothing	C/E grade PHED data ... Dermal = 8 replicates ... Inhalation = 8 replica... (Low confidence in the...

a Standard Assumptions based on an 8 hour work day as estimated by OREB. BEAD data were not available

b Mixer/Loader exposures are not appropriate for all application equipment scenarios as indicated in T scenario (i.e., the hazards are calculated for the scenario which has the maximum, daily cumulative

** In FMC's "Ethion Risk Mitigation Proposal", the Registrant proposed to prohibit erial applications;

Table V: Summary of Exposure and Margins of Exposure Values for Ethion[a]

Exposure Scenario (Scen. #)	Daily Dermal Dose[a] (mg/kg/day)	Daily Inhalation Dose (mg/kg/day)	Combined Dermal and Inhalation (mg/kg/day)	MOE Calculations
Mixer/Loader Exposures[a]				
Open Mixing Liquids For Aerial Application (I)	1.88	1.0×10^{-3}	1.88	0.40
Open Mixing Liquids For Ground-Based Applications (II)	0.43	2.3×10^{-4}	0.43	1.77
Applicator Exposures				
Groundboom Application (III)	0.03	7.4×10^{-4}	0.03	25.25
Airblast Application (IV)	0.82	5.1×10^{-4}	0.82	0.92
Aerial Application (V)	0.06	5.0×10^{-4}	0.06	12.6
High Pressure Handwand Application (VI)	0.76	3×10^{-5}	0.76	1.0
Mixer/Loader/Applicator Exposures				
Mixing/Loading and Application with a Backpack Sprayer (VII)	0.11	3.5×10^{-4}	0.11	6.89
Mixing/Loading and Application with a Low Pressure Handwand Sprayer (VIII)	1.47	2.2×10^{-4}	1.47	0.51
Mixing/Loading and Application with a Hose-End Sprayer(IX)	1.80	$<1 \times 10^{-5}$	1.80	0.42

Double #s

a Daily dose (mg/kg/day) = [Unit Exposure (mg/lb ai) * Max. Appl. Rate (lb ai/treatment) * Max. Treated/70 kg].

b MOE = NOEL/(Exposure * Dermal Absorption) for Ethion the MOE = 0.05 mg/kg/day / (Exposure above * 6.6%) (see Dose Response Section for details).

3.3

As part of the risk mitigation the registrant proposed to use enclosed cabs and a closed loading system for airblast application. An exposure assessment was conducted for workers using an application rate of 2.5 lb ai/acre. Using PHED Version 1.1, the mixer/loader using a closed system is exposed to 0.026 mg/kg/day ethion and the applicator performing an airblast application in an enclosed cab is exposed to 0.012 mg/kg/day ethion.

Post-Application Exposure

Post-application exposure (i.e., reentry) study requirements are addressed by Subdivision K of the Pesticide Assessment Guidelines. Post-application dermal and inhalation exposure monitoring along with concurrent soil and foliar residue dissipation data were required in the 1989 *Registration Standard for Products Containing Ethion*. The required data have not been submitted by the registrant. Data for several use patterns were required including terrestrial food, terrestrial non-food, greenhouse non-food, and domestic outdoor. Because citrus use is the only use being supported in reregistration, only those data pertaining to this terrestrial food use are still required.

A document entitled "Margin of Safety Risk Assessment Based on Surrogate Exposure Models for Workers Reentering Citrus Treated With Ethion Insecticide/Miticide, Revision No. 1" (EPA MRID 415089-01) was submitted to the Agency in support of Subdivision K requirements for the reregistration of ethion. The risk assessment is unacceptable because of several major inadequacies, including:

- there was a general lack of organization and references,

- critical data used in the risk assessment were not properly documented (i.e., the data source used by the investigator was not available to the Agency for review and/or verification), and

- foliar dislodgeable residue levels were combined for the assessment in a manner which is technically unacceptable (i.e., combined dry and wet season data to obtain representative levels).

Based on the toxicological endpoints and the potential for reentry exposure, the following data are required for reregistration:

GL# 132-1a. Foliar dislodgeable dissipation: Data are required for Orchard type crops (at least one representative site, i.e., oranges).

GL# 133-3. Estimation of dermal exposure: Data are required for Orchard type crops (at least one representative site, i.e., oranges).

GL# 133-4. Estimation of inhalation exposure: Data are required for Orchard type crops (at least one representative site, i.e., oranges).

Restricted Entry Interval

Data from the submission entitled, "Margins of Sfety Risk Assessment Based on Surrogate Exposure Models for Workers Reentering Citrus Treated with Ethion Insecticide/Miticide, Revision No. 1" was used in determining the appropriate restricted entry interval. Based on the toxicological database re-evaluation (refer to Dose Response section) and the reduced maximum application rate (2.5 lb a.i./A), the restricted interval was recalculated and the results supported maintaining a 21 day REI.

b. Occupational and Residential Risk Characterization

The Margins of Exposure (MOE) are summarized above in Table V. The MOE is an estimate of risk. MOEs are a ratio of the NOEL (in this case the LOEL) of 0.05 mg/kg/day and exposure times the dermal absorption rate.

MOE = NOEL (mg/kg/day) / [Exposure (mg/kg/day) X dermal absorption]

For ethion, an MOE of less than 100 is considered a risk concern. The MOEs for all mixer/loader and/or applicator scenarios are less than 100. With regard to the restricted entry interval, based on an MOE of 100 the calculated REI for citrus is 21 days.

In addition, the registrant proposed to use enclosed cabs and closed loading system for airblast application. An exposure assessment was conducted for workers using an application rate of 2.5 lb ai/acre. Using PHED Version 1.1, and using a LOEL of 0.05 mg/kg/day and a dermal absorption rate of 6.6%, the MOE for the mixer/loader (for closed systems) exposed to 0.026 mg/kg/day would be 29, and the MOE for the applicator in an enclosed cab would be 63.

Incorporating risk mitigation (i.e. lowering the rate of application) and considering the dermal absorption the moderately conservative risk estimates indicate that there is a risk concern for all workers.

There are no residential uses for this chemical; therefore, no exposure or risk is expected.

4. **Dietary Exposure and Risk Characterization**

a. Dietary Exposure

GLN 171-4 (a): Plant Metabolism : The qualitative nature of the residue in citrus is adequately understood based on an acceptable orange study. Based on the data, residues are not translocated from treated leaves or fruits. Residues in oranges are found primarily in the peel, and ethion *per se* is the major (ca. 70-80%) terminal residue. Ethion monooxon and ethion dioxon are minor metabolites accounting for <1% of the terminal residue on the day of treatment and 9% and 3% respectively, 90 days post-treatment (MRID#s 00155869, 00155870).

GLN 171-4 (b): Animal Metabolism - Ruminants : The qualitative nature of the residue in ruminants is adequately understood based on an adequate goat metabolism study. In the ruminant metabolism study, goats were dosed with [^{14}C]ethoxy-labeled ethion at 25 ppm in the diet (3x the maximum theoretical dietary burden). [Note: Maximum dietary burden is 8.25 ppm based solely on 33% dried citrus pulp in ruminant diet at 25 ppm.] In milk, the majority of radioactivity (>88%) is incorporated into natural constituents (fatty acids, proteins, and sugars). Ethion and O,O-diethyl phosphate (EOOP) are minor metabolites in milk accounting for 2.8 and 0.7% of the terminal residue, respectively. In fat, the majority of the residue (>70%) is incorporated into fatty acids, but ethion accounts for approximately 18% of the terminal residue. In kidney, the predominant metabolite is O,O-diethyl phosphate (EOOP; 51.5% TRR). The sodium salt of O,O-diethyl phosphoro-thionate (ESOP) and O,O-diethylphosphorodithioic acid (ESSP) are minor metabolites in kidney accounting for 7.0% and 3.3% of the terminal residue, respectively. Only trace levels of ethion (0.2% TRR), ethion monooxon (0.2% TRR), ethion dioxon (0.2% TRR), O,O-diethyl-S-(methylsulfinyl) methylphosphorodithioate (FMC 78152; 0.2% TRR), and O,O'-diethyl-S[(methylthio)methyl] phosphorodi-thioate (FMC 78153; 0.2% TRR) are found in the kidney. In muscle, ethion and O,O-diethyl phosphate (EOOP) are the major metabolites accounting for as much as 8.4% and 10.6% of the terminal residue. The sodium salt of O,O-diethyl phosphorothionate (ESOP) is a minor metabolite in muscle accounting for as much as 3.8% of the terminal residue and a trace level of O,O-diethylphosphorodithioic acid (ESSP; 0.5% TRR) is also present. In liver, the predominant metabolite is O,O-diethyl phosphate (EOOP; 41.2% TRR). Minor metabolites found in liver include ethion (0.1% TRR), ethion monooxon (0.4% TRR), ethion dioxon (0.3% TRR), O,O-diethyl-S-(methylsulfinyl) methylphosphorodithioate (FMC 78152; 0.3% TRR), O,O-diethylphosphorodithioic acid (ESSP; 0.7% TRR), the sodium salt of O,O-diethyl phosphorothionate (ESOP; 0.7% TRR), and monoethyl phosphate (MEP; 0.5% TRR). A significant portion of the terminal residue in liver has been characterized as unknowns (25.8% TRR); however, each unknown has been

identified as a distinct component that individually accounted for ≤7.7% of the terminal residue (MRID#s 00073144, 00155874, 42113702, 42113703, 42113704).

GLN 171-4 (b): Animal Metabolism - Poultry: The qualitative nature of the residue in poultry is not adequately understood (MRID# 00155875). However, data on the qualitative nature of the residue in poultry is not required for this reregistration eligibility decision since citrus is not currently recognized by the Agency as a poultry feed item.

GLN 171-4 (c) and (d): Residue Analytical Methods-Plants and Animals: An adequate method for purposes of enforcement of ethion tolerances in plant and animal commodities is available. The GLC/FPD method for determining ethion and ethion monooxon residues as distinct components is described in the Pesticide Analytical Manual (PAM), Vol. II, as Method I. This method is the organophosphate method formerly listed in PAM, Vol. I as multiresidue Protocol II. In this method, acetone extracts of 50-g macerated samples are extracted twice with methylene chloride, concentrated, mixed with acetonitrile, cleaned up on a polyethylene-coated alumina column, eluted with 60:40 (v:v) acetonitrile and water, extracted with methylene chloride, and analyzed with a gas chromatograph (CG) equipped with a flame photometric detector (FPD). Sensitivity is stated as 0.10 ppm for residues of ethion and ethion monooxon based on a 50 gram sample. Analytical methods deemed adequate by the Agency for data collection were used to generate the citrus field trial data, citrus processing data and meat and milk data submitted in support of the reregistration of ethion (MRID#s 00034468, 00073062, 00073094, 00073100, 00073105, 00073106, 00073141, 00073143, 00073147, 00073173, 00073811, 00073812, 00109285, 00155850, 42411403, 42833401).

PESTDATA (PAM, Vol. I, Appendix II) contains data concerning the applicability of all FDA multiresidue methods for recovery of ethion and ethion monooxon. Ethion is completely recovered (>80%) using PAM Vol. I multiresidue Protocols I, II, and III. Ethion monooxon is completely recovered using Protocols II and III.

Additional data are required as confirmatory information. A representative sample from the goat metabolism study (MRIDs 42113702 through 42113704) must be analyzed using the preferred enforcement method. The Agency has favorably reviewed a protocol submitted by the registrant concerning the conduct of the radiovalidation study.

GLN 171-4 (e): Storage Stability: (MRID#s 00073152, 00155504, 42411401, 42411402, 42833401) Adequate storage stability data on ethion residues are available to support the storage conditions and intervals of samples from

magnitude of the residue studies on citrus fruits. Residues of ethion and ethion monooxon are stable in/on oranges at -15°C to -25°C for up to 38 months and in/on lemons and grapefruit for approximately 15 months. Storage stability data for the processed commodities of citrus reflecting up to 12 months of storage at -18°C are required to support citrus processing data (MRID 00155850) used for tolerance reassessment. Sample storage conditions and intervals must be reported for the meat and milk magnitude of the residue study (MRIDs 00073138 and 00073153) used for tolerance reassessment. Storage stability data which adequately reflect meat and milk sample storage conditions and intervals are also required. All required data are considered confirmatory since available data indicate that reasonable diligence was exercised in the conduct of the subject studies to ensure that magnitude of the residue results were not invalidated due to sample storage and since existing evidence indicates that residues of ethion and ethion monooxon are relatively stable in unprocessed frozen citrus over long storage intervals.

GLN 171-4 (k): Magnitude of the Residue in Plants: (MRID#s 00073143, 00155580, 00155850, 42411407, 42411408, 42833401 42411409, 42411410, 42411411, 42411412, 42411404, 42411405, 42411406) Data submitted to fulfill this requirement are adequate to reassess the tolerances for residues of ethion in/on citrus fruits. The use of ethion on citrus grown in Florida and Texas only is supported by acceptable field residue data from trials reflecting the maximum registered use pattern. The submitted citrus field trial data indicate that the current tolerance level for ethion residues of concern in/on citrus fruits should be increased to 5 ppm.

GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed: Data submitted to fulfill this requirement are adequate to determine the extent to which residues of ethion concentrate in processed citrus products (MRID# 00155850). An adequate citrus processing study indicates that the combined residues of ethion and ethion monooxon concentrate up to 10.8 times in citrus oil and 4.3 times in dehydrated citrus pulp processed from ethion-treated fruit (MRID# 00155850). Consequently, the Agency has recommended that the established feed additive tolerance in dehydrated citrus pulp be increased from 10 to 25 ppm and that a food additive tolerance should be established in citrus oil at 55 ppm. Pending submission of acceptable storage stability data on processed citrus commodities, no additional data are required.

GLN 171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs: Cattle feeding studies were reviewed in the Registration Standard (9/82). Cows were fed ethion at rates of 5.0 ppm (0.8x), 10.0 ppm (1.6x), and 20.0 ppm (3.2x) for 30 days. [Note: Maximum dietary burden of 6.25 ppm based solely on 25% dried citrus pulp in ruminant diet at 25 ppm.] Milk collected from cows fed at 5

and 20 ppm contained ethion residues of <0.005-0.009 ppm and <0.005-0.034 ppm, respectively. Muscle and fat tissue collected from cows fed 20 ppm contained ethion residues of 0.008 ppm and 0.222 ppm, respectively. Ethion residues were nondetectable (<0.005 ppm) in kidney and liver tissues from cattle fed with ethion at all levels and in muscle tissues from cattle fed at 5 and 10 ppm. Ethion monooxon and dioxon residues were nondetectable (<0.005 and <0.01 ppm, respectively) in milk or tissues from cows fed at all levels (MRID#s 00073138, 00073153, 00155850). Based on the available ruminant feeding study, tolerances on cattle fat (2.5 ppm), meat (2.5 ppm), and meat by-products (1.0 ppm) are too high and should be lowered to 0.2 ppm to be consistent with tolerances established on other ruminant animal commodities. [Note: Tolerances on cattle meat, meat by-products, and fat were established for the use of ethion as a cattle dip in Australia; however, this use has not been supported in reregistration.] Storage stability data to support these data are outstanding. These storage stability data are considered confirmatory since available data indicate that reasonable diligence was exercised in the conduct of the subject studies to ensure that magnitude of the residue results were not invalidated due to sample storage and since existing evidence indicates that residues of ethion and ethion monooxon are relatively stable in unprocessed frozen citrus for long storage intervals. Pending the receipt of adequate storage stability data, the Agency considers the available information adequate to reassess the current tolerances on meat and milk.

Citrus is not currently recognized by the Agency as a poultry feed item. the Agency recommends that the established tolerances listed in 40 CFR §180.173 for eggs and poultry meat, meat by-products, and fat be revoked at this time.

GLN 171-5 Residue Reduction: These data were required by the Agency on a variety of commodities while in transit and storage and after cooking, peeling and washing to permit a more accurate assessment of acute exposure resulting from consumption of commodities treated with ethion. the Agency granted a waiver from this data requirement because the use pattern will be restricted to application on citrus only.

GLN 165-1 Confined Rotational Crops: The Agency has granted a waiver from this data requirement because use pattern will be restricted to application on citrus only. Citrus is not a rotated crop.

GLN 165-2 Field Rotational Crops: N/A.

b. Dietary Risk Characterization

The chronic dietary risk assessment of ethion was conducted using the

RfD of 0.0005 mg/kg body weight/day (discussed previously). Two chronic dietary risk assessments were performed. First, published uses plus the reassessed tolerances were considered. Second, only the uses being recommended in reregistration were considered (with the exception of an import tolerance on cattle, which was included even though not supported in reregistration). Both tolerance-level residues and anticipated residues were considered in each analysis. Data on percent crop treated were not used directly, since percent of crop treated information should already be reflected in the FDA monitoring data used to estimate anticipated residues.

Chronic Exposure and Risk

The exposure estimate for all currently published uses (including reassessed tolerances and excluding the import tolerance) is provided as a worst-case scenario. Based on tolerance level residues from published tolerances and tolerance reassessments, the Theoretical Maximum Residue Contribution (TMRC) of ethion in the diet of the U.S. population as a whole was 0.020365 mg/kg bodyweight per day or 4073% of the RfD. The TMRC for the subgroup Non-nursing Infants (Less Than One Year Old), the subgroup with the highest estimated exposure, was 0.054200 mg/kg bodyweight per day, or 10,840% of the RfD. The exposure and corresponding percent of reference dose based on Anticipated Residue Contribution (ARC) for the overall U.S. population from published uses, including reregistration tolerance reassessments, are listed below.

Population Subgroups	Exposure (mg/kg/day)	% Reference Dose
U.S. Population	0.000496	99
Females 13+ years, nursing	0.000699	140
Children (1-6 years)	0.000596	120
Southern Region	0.000596	119
U.S. population-summer season	0.000538	108
Non-Hispanic, Others	0.000519	104

For most of the subgroups the %RfD is high due to the exposure contribution from tea, e.g., 65% for the U.S. population subgroup and 116% for the females ages 13+, nursing subgroup. The tolerance for tea is not being supported in the reregistration of ethion.

From only the Uses Recommended in Reregistration (plus Imported Tolerance)

The Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population from published tolerances being supported in reregistration are listed below. Tolerances levels for the cattle dip use were included here even though this use is not supported in reregistration, because it is currently an import tolerance.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.016279	3258
Non-nursing Infants	0.029628	5926

The exposure and corresponding percent of reference dose based on Anticipated Residue Contribution (ARC) for the overall U.S. population from published uses supported in reregistration are listed below. Anticipated residues for the cattle dip use were included here even though this use is not supported in reregistration, because it is currently an import tolerance.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.000044	9
Children (1-6 years)	0.000081	16

Based on the estimated exposures/percent RfD values, the chronic dietary risk posed by ethion is not of concern when only the commodities recommended in reregistration (but including the import tolerance for cattle) are considered; the ARCs for the U.S. population and all population subgroups are well below the Reference Dose. The percent of the Reference Dose would be even lower if the import tolerance were not included.

Acute Dietary Exposure and Risk

The detailed acute dietary exposure analysis evaluates individual food consumption as reported by respondents in the USDA 77-78 Nationwide Food Consumption Survey (NFCS) and estimates the distribution of single day exposures through the diet for the U.S. population and certain subgroups. The analysis assumes uniform distribution of ethion in the commodity supply. Since the toxicological effect to which high-end exposure is being compared to in this analysis is cholinesterase inhibition, all population subgroups are of concern. For pesticides in which acute NOELs are based on human studies, the Agency generally is not concerned unless the MOE is below 10. For Ethion, the

toxicological endpoint is based on a LOEL from a human study. Because the effects were observed on the 19th day, and this endpoint is for a one day, acute dietary exposure, an MOE of 10 or below being a concern is still appropriate.

In a previous ethion dietary exposure analysis in support of the RED, HED/CBRS recommended for an increase in the tolerance for the citrus fruits group from 2.0 ppm to 5.0 ppm. In the dietary analysis for the RED, acute anticipated residues (ARs) for pulp and peel of citrus as well as acute ARs for meat and milk were incorporated into the analysis. The analysis resulted in MOEs which were below 10. Further refinement of the ethion residue were provided. The following acute dietary analysis includes the latest refinements of the residues (6/29/95).

Food uses evaluated in this analysis were only the uses of ethion supported in reregistration, that is, a citrus group tolerance in Florida and Texas and meat and milk tolerances. There are numerous other tolerances still registered in 40 CFR §180.173, 185.2750 and 186.2750. Anticipated residue estimates for ethion residues of concern were generated using an available feeding study (MRID 00073138 and 00073153) and a proposed feed additive tolerance for residues of ethion in dried citrus pulp (25ppm) for the determination of ethion acute anticipated residue level estimates for meat and milk. Calculated ethion concentration/reduction factors for citrus peel (6.2x) and citrus pulp (0.02x) were used in conjunction with the proposed tolerance increase (5.0 ppm) to determine the ethion acute anticipated residue level estimates for the citrus group.

Further acute anticipated residues have recently been provided for citrus juices. Since some juices tend to be mixed before consumption and some juices are freshly squeezed by consumers, this dietary analysis included two different residue approaches. For juices which are typically mixed, the average anticipated residue for the fruit will be multiplied by the average processing factor for the fruit. Since it is not uncommon to squeeze your own orange or lemon juice, a more conservative anticipated residue, but less conservative than the tolerance level was calculated by multiplying the highest average residue value found in the field trial study by the average processing factor.

The following residues are shown in comparison to the tolerance level for citrus.

Commodity	Tolerance level	Acute AR
Citrus peel	5.0 ppm	31.0 ppm
Citrus pulp	5.0 ppm	0.1 ppm
Tangerine juice	5.0 ppm	0.175 ppm

Lemon juice	5.0 ppm	0.224 ppm
Grapefruit juice	5.0 ppm	0.119 ppm
Lime juice	5.0 ppm	0.154 ppm
Orange juice	5.0 ppm	0.231 ppm

The following are the values of average or highest average field trial residue and average processing factor for the citrus group. The acute anticipated residue for the juice is also listed.

Average AR		Average Processing Factor	Acute AR for juice
Grapefruit	1.7 ppm	0.07	0.119 ppm
Lime	2.2 ppm	0.07	0.154 ppm
Tangerine	2.5 ppm	0.07	0.175 ppm
Highest Average Field Trial Residue			
Orange	3.3 ppm	0.07	0.231 ppm
Lemon	3.2 ppm	0.07	0.224 ppm

Summaries of the acute dietary risk for the various population subgroups are as follows (Table VI)

Table VI: Acute Dietary Exposure Analysis - Margins of Exposure (MOE)

Population Subgroup	High End MOE	MOE (Percentile)
U.S. pop.-48 states	7	17 (98th)
Infants (< 1 year)	**3**	13 (95th)
Children(1-6 years)	3	10 (97th)
Females(13+ years)	10	25 (98th)
Males(13+ years)	13	50 (95th)